IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application Number	:	09/720,096	Confirmation No.: 6906
Applicant	:	Dan Nilsson, *et al.*	
Filed	:	February 1, 2001	
Title	:	METHOD OF PREVENTING BACTERIOPHAGE INFECTION OF BACTERIAL CULTURES	
TC/Art Unit	:	1656	
Examiner:	:	David J. Steadman, Ph.D.	
Docket No.	:	54337.000009	
Customer No.	:	**21967**	

ARGUMENTS ACCOMPANYING PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

Applicants hereby submit the following Arguments, in five (5) or less total pages, as attachment to the Pre-Appeal Brief Request for Review (Form PTO/SB/33). A Notice of Appeal and Petition for Extension of Time are concurrently filed. The Commissioner is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. **50-0206**.

Summary

Claims 1, 9-11, 17, 24, 28, 30-32, 34, 36-37, 39, and 41-43 under 35 U.S.C. § 103(a) have been rejected as allegedly unpatentable over Dickely *et al.* (U.S. Pat. 5,691,185; hereafter "Dickely '185") in combination with various secondary references. The claims at issue relate to methods for fermentation and acidification using non-proliferating bacterial strains, which resist bacteriophage attack. It is undisputed that the cited references only disclose fermentation using proliferating bacterial strains. By contrast, Dickely '185, discloses the existence of a non-proliferating strain, and its conversion into a proliferating strain (by a genetic modification) and using the resulting proliferating strain for fermentation. Notwithstanding these differences, the Examiner has alleged obviousness over these references. Applicants respectfully request withdrawal of the rejections and allowance of the claims for the reasons stated below.

Arguments

Claims 1, 9-10, 17, 24, 30-31, 37, and 43-44 have been rejected as allegedly obvious over Dickely '185 as evidenced by Luksas (U.S. Pat. 3,720,520; hereafter "Luksas"). Luksas is only cited for the proposition (undisputed) that milk is one product for cheese flavoring as recited in claim 31..

Dickely '185 teaches a method for derivation of a Pur- bacterial strain which includes identification of Pur- strains by their inability to grow in a defined medium that has been treated to remove all residual purines ("DN medium"). *See* Dickely, Example 8 (cols. 26-27) and Dickely *et al.*, Mol Microbiol. 1995 Mar;15(5):839-47 (of record, see IDS submitted December 21, 2000; hereinafter, "Dickely NPL"), pg. 845, left column (describing preparation of DN medium). The Examiner has alleged that it would have been obvious to modify the reference disclosure by substituting milk for the DN medium. However, Dickely '185 only teaches use of a medium that has been treated to remove all residual purines. There is no evidence of whether there was any known method of treating milk to remove any residual purines without also impairing its ability to support growth of the desired bacterial strains. Even if such methods were known, the Examiner has not given any reason for one of ordinary skill in the art to abandon the reliable methods taught by Dickely '185 in favor of the untested methodology proposed by the Examiner. Thus, the rejection is improper as the proposed modification is unsupported by any valid scientific reasoning or evidence.

Even if it were obvious to substitute milk for the treated medium taught by Dickely '185 (which Applicants dispute), there is no evidence that any measurable acidification or fermentation would occur during the isolation or testing of a Pur- strain. Thus, the rejection further depends on the Examiner's position that the claims do not require any acidification or fermentation to occur. This rejection is improper because each of the independent claims recite a method that includes adding bacteria to a substrate and keeping that substrate under conditions where acidification or fermentation of that substrate occurs. For example, claim 1 recites "[a] method of fermenting milk comprising adding a cultured purine or thymidine auxotrophic bacterial strain to milk and keeping the milk under conditions where the bacterial culture is able to acidify the milk, wherein said auxotrophic bacterial strain is non-proliferating in the milk" (emphasis added). The claim sets forth sufficient conditions for acidification to occur, namely the adding of bacteria to milk and keeping the milk under conditions where the bacterial culture is able to acidify the milk. It is tautological that acidification results when the milk is kept under conditions where the bacterial culture is able to

acidify the milk. The Examiner has further alleged that the claims do not recite any temporal limitation to achieve the acidification of milk, however, in the step of "keeping the milk under conditions. . . " the act of "keeping" includes whatever time is required. The purported interpretations of independent claims 30 and 31 are similarly unreasonable. .

As an alternative interpretation of claims 30, 31, and their dependents, the Examiner alleges that if fermentation is part of the claimed method, then breakdown of as few as two individual organic molecules would suffice. The sole alleged justification for this interpretation is a statement in the specification that fermentation "relates to any aerobic or anaerobic breakdown of organic compounds by a bacterial culture with the production of an end product." Specification, pg. 6, lines 4-5 (emphasis added). However, the Examiner has improperly equated "relates to" with "is defined as." If there were any suspicion that a definition might have been intended, this would be precluded by use of the word "fermentation" throughout the specification in a manner inconsistent with the Examiner's proposed definition. For example, the specification describes the problem of "fermentation failure" resulting when bacteria are added to milk but are then killed by bacteriophages. Specification, pg. 3. Since bacteria remain metabolically active for some time after viral infection (during which the normal metabolic machinery are co-opted for production of more bacteriophages) it is clear that "fermentation" as the Examiner has defined it would still occur, yet the specification describes this as "fermentation failure." Thus, the term "fermentation" should be interpreted as that term is used in the art since there is no clearly expressed intent to do otherwise. *See, e.g., Merck v. Teva*, 395 F.3d 1364, 1370 (Fed. Cir. 2005). Accordingly, the rejections of claims 30 and 31 (which recite the term "ferment") are based on an improper interpretation.

Similarly, as to claim 1, the Examiner has proposed defining acidification, "[i]n line with this definition [of fermentation]," to require only the breakdown of two organic molecules to yield acidic products. Office Action mailed March 30, 2010, page 11. Applicants vigorously dispute that the term "fermentation" had been given the special definition proposed by the Examiner. However, even if one of the claim terms had been given a special definition, there is no principle of logic or of law that would justify attempting to extrapolating from that one special definition and redefining other related terms. Rather, absent any clearly expressed intent to the contrary, the claim terms (including "acidify") retain their ordinary interpretation. *Merck v. Teva* at 1364. Accordingly, the rejection of claim 1 (and its dependents) is also based on an improper interpretation.

Claims 11, 34, 36, 39, and 41-42 have been rejected as allegedly obvious over Dickely '185 as evidenced by Luksas and in further view of Barach *et al.*, U.S. Pat. 4,294,930 (hereinafter, Barach) as evidenced by Groboillot *et al.*, *Biotechnol. Bioengineer.* 42:1157–1163 (1993) (hereinafter, Groboillot). Barach and Groboillot do not remedy any of the deficiencies of Dickely '185 and Luksas discussed above. Because claims 11, 34, 36, 39, and 41-42, each properly depend from claim 1 or 31, they are not obvious for at least the reasons stated above with those claims.

Further, as to **claims 11 and 42**, the Examiner has alleged that it would have been obvious to further modify the teachings of Dickely '185 to test whether a strain is Pur- by performing a growth test using an inoculum of 10^8 CFU/mL. The Examiner has further alleged that "[o]ne would have been motivated to use 10^8 CFU/mL of the culture of the [purine auxotrophic] strain because Barach teaches this is desirable." Office Action mailed March 30, 2010, page 13. However, Barach does not teach that this inoculum is desirable for any other purpose than using a proliferating strain for fermentation of milk. Particularly, there is no justification given for modifying a method for testing growth potential a Pur- strain by incorporating an inoculum taught for fermentation. Rather, Dickely NPL teaches away from using such a high inoculum of a Pur- strain. Specifically, Dickely NPL teaches that spontaneous Pur+ revertants arise with a frequency of approximately 1 in 10^6 viable cells. *See* Dickely NPL, pg. 842, right col. Since obtaining and testing Pur- strains is the goal of the Dickely '185 method, one of ordinary skill in the art would have used a much lower inoculum than 10^6 cells to avoid obtaining Pur+ revertants, and therefore would not have used the high inoculum taught by Barach. Thus, claims 11 and 42 are not obvious for the further reason that the rejection is based on an improper combination of reference disclosures.

As to **claims 34 and 39**, the purported motivation for performing the recited steps is "to achieve 10^8 CFU/mL of the culture for growth analysis" as allegedly taught by Barach. However, as with claims 11 and 42, Barach does not provide any valid justification for using this inoculum, and the Office Action has not stated a valid *prima facie* case of obviousness against these claims.

As to **claims 36 and 41**, the Examiner has taken the position that acidification to pH less than or equal to 5.0 would be the inherent result of inoculating a Pur- bacterium into milk to test growth ability. However, the specification teaches that acidification depends on using a sufficient inoculum. *See* pg. 17-18. Figure 1 graphically illustrates the relationship between rate of acidification and inoculum. In this figure, percentages referred to dilution of an outgrown culture, *i.e.*, 50% means an

outgrown culture was washed and resuspended in twice its original volume. Acidification to pH less than 5.5 was only observed with the highest inoculums tested (50% and 25%) and not with 10% or 1% inoculums. Even if one of ordinary skill in the art were to use milk as a medium to test growth ability (which is unjustified for the reasons stated above), there is no reason to use an inoculum that would be high enough to result in acidification to pH 5.0. Rather, one of ordinary skill in the art would have used a much lower inoculum because Dickely NPL teaches that spontaneous Pur+ revertants arose with a frequency of approximately 1 in 10^6 viable cells. *See* Dickely NPL, pg. 842, right col. A growth test would give an invalid result if a high inoculum were used because spontaneous revertants would overtake the culture. To obtain a valid growth test result, one of ordinary skill in the art would instead use a much lower inoculum, such as 0.0001% or even lower, yet there is no evidence to suggest that such a minimal inoculum could acidify milk to the recited pH within the contemplated time-frame (100 hours in the Examiner's proposed modification of the references). Accordingly, acidification to pH less than or equal to 5.0, as recited in the claims, would not be the inherent result of the Examiner's proposed modification of the reference disclosure.

Claims 28 and 32 have been rejected as allegedly obvious over Dickely '185 as evidenced by Luksas as applied to claims 1, 9-10, 17, 24, 30, 33, 37, and 43 above and in further view of Nilsson *et al.* (*Mol. Gen. Genet.* 235:359-364, 1992; hereafter "Nilsson"), or Jochimsen *et al.* (*Mol. Gen. Genet.*, 143:85-91, 1975; hereafter "Jochimsen"), respectively. However, Nilsson and Jochimsen fail to remedy any of the aforementioned deficiencies of Dickely '185 and Luksas, and accordingly claims 28 and 32 are not obvious over these references for at least the reasons stated above with claim 1 (from which claims 28 and 32 depend).

Respectfully submitted,
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Dated: 8/30/10

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